Breast Cancer beyond the Age of Mutation.

Journal: Gerontology

Publication Year: 2015

Authors: Mark A LaBarge, E Lorena Mora-Blanco, Susan Samson, Masaru Miyano

PubMed link: 26539838

Funding Grants: Interdisciplinary Training in Stem Cell Biology, Engineering and Medicine

Public Summary:
Age is the greatest risk factor for breast cancer, but the reasons underlying this association are unclear. While there is undeniably a genetic component to all cancers, the accumulation of mutations with age is insufficient to explain the age-dependent increase in breast cancer incidence. The process of aging is associated with gradual breast tissue changes that not only corrupt the tumor-suppressive activity of normal tissue but also impose age-specific changes in gene expression that alter the tissue microenvironment. Here we propose a model to better understand the respective roles played by somatic mutation, microenvironment, and epigenetics making women more susceptible to breast cancer with age.

Scientific Abstract:
Age is the greatest risk factor for breast cancer, but the reasons underlying this association are unclear. While there is undeniably a genetic component to all cancers, the accumulation of mutations with age is insufficient to explain the age-dependent increase in breast cancer incidence. In this viewpoint, we propose a multilevel framework to better understand the respective roles played by somatic mutation, microenvironment, and epigenetics making women more susceptible to breast cancer with age. The process of aging is associated with gradual breast tissue changes that not only corrupt the tumor-suppressive activity of normal tissue but also impose age-specific epigenetic changes that alter gene expression, thus reinforcing cellular phenotypes that are associated with a continuum of age-related tissue microenvironments. The evidence discussed here suggests that while the riddle of whether epigenetics drives microenvironmental changes, or whether changes in the microenvironment alter heritable cellular memory has not been solved, a path has been cleared enabling functional analysis leading to the prediction of key nodes in the network that link the microenvironment with the epigenome. The hypothesis that the accumulation of somatic mutations with age drives the age-related increase in breast cancer incidence, if correct, has a somewhat nihilistic conclusion, namely that cancers will be impossible to avoid. Alternatively, if microenvironment-driven epigenetic changes are the key to explaining susceptibility to age-related breast cancers, then there is hope that primary prevention is possible because epigenomes are relatively malleable.

Source URL: http://www.cirm.ca.gov/about-cirm/publications/breast-cancer-beyond-age-mutation